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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/494,332	01/28/00	GORMAN	K

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EXAMINER	
GOLDBERG, J	
ART UNIT	**PAPER NUMBER**
1655	10

DATE MAILED: 12/14/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/494,332	Applicant(s) GORMAN ET AL.	
	Examiner Jeanine A Enewold Goldberg	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Priority

1. This application claims priority to 60/118,498, filed February 3, 1999.

However, an application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Specification

2. It is noted that SEQ ID NO: 10 and 1 are 100% identical. Furthermore, SEQ ID NO: 11 consists of 24 of the 25 nucleotides of SEQ ID NO: 2.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-42 are indefinite because the claim appears to be describing a method of detecting both HCV and HIV, however, as written the claim may be directed to employing only HCV or HIV. For examples, it is unclear how the artisan would gather any information regarding HIV if only HCV products were produced. Thus it is unclear the metes and bounds of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1, 3-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (PNAS, Vol. 88, pg. 1711-1715, March 1991) and Backus et al (US Pat 6,001,558, December 1999) in view of Nedjar et al (J. of Virological Methods, Vol. 35, No. 3, pg. 297-304).

Han et al. (herein referred to as Han) teaches the sequence of 341 base pairs from the 5' untranslated region (UTR) of HCV and alignment of this sequence from several different HCV isolates. Han teaches extracting the plasma from HCV-positive or negative blood donors. RNA was isolated and converted into single-stranded cDNA by reverse trancriptase using the appropriate cDNA primer (pg. 1711, col. 2). Han teaches primers for the PCR amplification of 5' UTR and means of cloning these PCR products (pg. 1711, col. 2, and Figure 2). The PCR products were analyzed by southern blot hybridization using a labeled oligonucleotide probe (pg. 1711, col. 2). Han teaches that when the sequence of the 5' UTR is compared among isolates, there is a high degree of sequence homology and that the sequence mismatches that are present are clustered in 5 positions, as taught in Figure 2 (see also pg. 1713, para 1). Han teaches that the 342 base pair 5' UTR sequence represents a signature sequence that could serve as a

HCV-specific DNA probe for the detection of all strains of the virus and further that the primers and highly reliable PCR protocol method as taught could be used for this purpose (pg. 1714, para 4).

Backus et al. (herein referred to as Backus) teaches amplification and detection of HIV-1 and HIV-2. Backus teaches oligonucleotides which amplify HIV-1 nucleic acids including oligonucleotides which are SEQ ID NO: 3 and 5. Backus also teaches an oligonucleotide which comprises the nucleotides of SEQ ID NO: 4. Backus, furthermore, teaches oligonucleotides which amplify HIV-2 nucleic acids including oligonucleotides which are SEQ ID NO: 6 and 7. Backus also teaches oligonucleotide probes of SEQ ID NO: 13, 14 and 16 for HIV-1 and HIV-2. The primers chosen were from identified highly conserved sequence regions (col. 10, lines 50-60). Backus teaches that a biological sample is used which included cellular-or viral material, hair, body fluids, or cellular material containing nucleic acids which may be detected (limitations of Claims 8 and 23).

Han and Backus do not specifically teach co-amplifying or co-detecting HCV and HIV using the primers of the instant claimed invention.

However Nedjar teaches a method of co-amplification of specific sequences of HCV and HIV by using PCR assays. Nedjar teaches the ability to co-amplify specific sequence from two different viral genomes in the same reaction mixture offers the possibility of simultaneous detection and diagnosis of more than one viral agent in serum samples of infected individuals.

Further, in the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed oligonucleotides simply represent structural homologues of the full length disclosed 5' UTR HCV and the HIV-1/2 sequence concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited reference in the absence of secondary considerations. Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Han and Backus in view of Nedjar to obtain the claimed invention as a whole. The skilled artisan would have been motivated to have used primers from the 5' UTR region to detect HCV, as taught by Han and primers from HIV-1 and HIV-2 as taught by Backus. Since Han provides an alignment of several isolates which show conserved regions between the isolates, and delineates the ORFs, the ordinary artisan would have been motivated to have designed primers which amplify various regions of interest from the 5' UTR region. Specifically, the skilled artisan would have chosen SEQ ID NO: 1 and 2, which flank ORF3. Furthermore, the skilled artisan

would have chosen SEQ ID NO: 11, 12 or 13 for probing the detection of HCV. The ordinary artisan would have been motivated to amplify the 5' UTR region of HCV since Han teaches that the 342 base pair 5' UTR sequence represents a signature sequence that could serve as a HCV-specific DNA probe for the detection of all strains of the virus and further that the primers and highly reliable PCR protocol method as taught could be used for this purpose. The ordinary artisan would have used the probes and primers from Backus, based upon the detailed analysis provided that these probes and primers were for conserved regions among the numerous isolates. The ordinary artisan would have combined the teachings of Han and Backus in view of Nedjar for the express benefit of diagnosing more than one viral agent in samples of infected individuals. The ordinary artisan would have recognized that the detection of more than one viral agent would have been ideal for saving time, and reagents. The multiplexing of numerous primers into a single reaction has the express benefit of saving reagent by limiting the number of assays and also saving time of scientists since the results may be obtained simultaneously. Thus, the ordinary artisan would have combined the teachings of detecting HCV with the teachings of detecting HIV-1 and HIV-2.

5. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (PNAS, Vol. 88, pg. 1711-1715, March 1991) and Backus et al (US Pat 6,001,558, December 1999) in view of Nedjar et al (J. of Virological Methods, Vol. 35, No. 3, pg. 297-304) as applied to Claims 1, 3-15, 23 above, and further in view of Maertens et al (US Pat. 5,846,704, December 1998).

Neither Hans, Backus nor Nedjar specifically teach performing reverse transcriptase with random oligonucleotide primers.

However, Maertens et al teaches a method of genotyping of HCV isolates using probes targeting sequences from the 5' UTR region of HCV (abstract). Maertens teaches extracting viral DNA from serum such that RNA was pelleted (col. 24, lines 60-68)(limitations of Claim 8). Random primers were then added such that cDNA was synthesized (col. 24, lines 60-68)(limitations of Claim 2). Maertens teaches amplifying the cDNA with outer primers and subsequently inner primers (col. 25, lines 5-10).

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the extraction method of Han, or Backus with the extraction method of Maertens to obtain the claimed invention as a whole. The ordinary artisan would have realized that RNA may be transcribed using either random primers, as taught by Maertens, or primers corresponding to specific HCV or HIV RNA, as taught by Hans and Backus. Since the art teaches that RNA from HCV may be reverse transcribed using either random or specific primers, the ordinary artisan would have realized that they were equivalents and may have substituted random primers for primers corresponding to specific HCV and HIV regions.

6. Claims 31, 33, 35, 37, 39, 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Han et al (PNAS, Vol. 88, pg. 1711-1715, March 1991) and Backus et al (US Pat 6,001,558, December 1999) in view of Nedjar et al (J. of Virological Methods, Vol. 35, No. 3, pg. 297-304) as applied to Claim 1, 3-13, 40-42 above, and

further in view of Ahern (www.thescientist.library.upenn.edu/yr1995/july/tools_950724.htlm, December 22, 1998).

Neither Han, Backus nor Nedjar specifically teaches packaging necessary reagents into a kit.

However, Ahern teaches reagent kits offer scientists good return on investment. Ahern teaches kits save time and money because the kits already comes prepared.

Therefore, it would have been **prima facie** obvious to one of ordinary skill in the art at the time the invention was made to have modified the teachings of Han and Backus in view of Nedjar with the teachings of Ahern to incorporate the necessary reagents into a packaged kit. The ordinary artisan would have been motivated to have packaged the primers, probes, and reagents of Han and Backus into a kit, as taught by Ahern for the express purpose of saving time and money.

Allowable Subject Matter

7. The instant IPC region and primers to the synthetic region are novel over the prior art. The SEQ ID NO: 8, 9 and 15 are not previously known in the art. However, Picone et al. (US Pat. 5,491,225, February 1996) and Blasczyk et al (Beitrage Zur Infusionstherapie Und Transfusionmedizin, Vol. 34, pg. 236-241, 1997-abstract only) teach incorporating IPC RNA into an assay. Picone et al. (herein referred to as Picone) teaches "internal positive control oligonucleotide sequences" are a recombinant or synthetic oligonucleotides that ensure assay users that the amplification process has

occurred in the event that the sample being tested has no target nucleic acid. Additionally, Blasczyk et al. (herein referred to as Blascyzk) teaches a pair of primers which amplify a fragment of the human growth hormone gene was included as an internal positive amplification control. The presence or absence of specific PCR amplification allowed definite allele assignment without the need for any postamplification specificity step. Additionally, Blasczyk teaches that the internal positive control primers indicate a successful PCR amplification (abstract).

Thus, while the concept of internal control regions and primers to amplify are known in the art, the specific sequences of the instant used primers are novel.

Conclusion

8. No claims allowable.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) McDonough et al (US Pat. 5,712,385, January 1998) teaches detection of HIV-1. Among the oligonucleotides taught are SEQ ID NO: 5 and 13.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Enewold Goldberg
December 4, 2000

LISA B. ARTHUR
PRIMARY EXAMINER
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